# PROFILE MICROVASCULAR AND MACROVASCULAR COMPLICATION OF DIABETES MELLITUS IN WETLAND AREA: A STUDY FROM BEST-DIAB 2 (BORNEO WETLAND STUDY ON DIABETES 2)

**Venna Febrian K[1)], Adlan Fariz[1)], Achmad Muamar[1)], Nanang Miftah Fajari [2)]**

[1]Department of Internal Medicine, Faculty of Medicine, Lambung Mangkurat University, <Banjarmasin>
[2]Endocrine, Metabolic and Diabetes Division, Department of Internal Medicine, Faculty of Medicine, Lambung Mangkurat University, <Banjarmasin>

**Korespondensi**
ahmadmuamar2012@gmail.com

**ABSTRACT**
Diabetes mellitus is a disease that is strongly associated with microvascular and macrovascular complications that, if left untreated, can produce chronic complications that affect quality of life. A cross-sectional study with outpatients at the metabolic endocrine polyclinic of diabetes mellitus at Ulin General Hospital, Banjarmasin, as a population. A total of 545 data were collected during the 2019-2022 period. Macrovascular complications were hypertension 66.2%, DFU 23.9%, CAD 17.05%, and stroke/CVA 10.08%, while microvascular complications were diabetic retinopathy (78.6%), diabetic neuropathy (84.6%), diabetic nephropathy (14.9%), and erectile dysfunction (73.3%) in male patients. The most common microvascular complications are diabetic neuropathy in the majority of female patients and erectile dysfunction in all male patients. The most macrovascular complications are hypertension with the majority of female.

**KEYWORDS**
Diabetes Mellitus (DM); Macrovascular complications; Microvascular complications; Wetlands; Ulin general hospital; Banjarmasin

## INTRODUCTION

From various epidemiological studies it is clear that the incidence of Diabetes mellitus (DM) is increasing worldwide especially in developing countries such as Indonesia. If left untreated, DM can result in probability of chronic complications which may severely affect the quality of life. Diabetes is a disease that is strongly associated with both microvascular and macrovascular complications including retinopathy, nephropathy, and neuropathy (microvascular) and ischemic heart disease, peripheral vascular disease, and cerebrovascular disease (macrovascular), resulting in organ and tissue damage[1].

The pathologic hallmark of DM involves the vasculature leading to both microvascular and macrovascular complications. Diabetes-associated vascular alterations include anatomic, structural, and functional changes leading to multiorgan dysfunction. It is becoming increasingly important for physical therapists to be aware of diabetes-related vascular complications, early identification and management of diabetes mellitus in patients[1].

Therefore, this descriptive study on diabetes mellitus patients at metabolic endocrine polyclinic diabetes mellitus in Ulin Hospital Banjarmasin are to briefly describe the incidence and analyze various risk factors of microvascular and macrovascular events, so they can be managed properly and can prevent the worsening of the condition of the outpatient and improve their quality of life.

## RESEARCH METHOD

This cross-sectional study used data conducted by outpatients in metabolic endocrine polyclinic diabetes mellitus in Ulin Hospital Banjarmasin. The study will be narrated into a descriptive study that describes the profile of Microvascular and Macrovascular Complication of Diabetes Mellitus in Wetland Area: A Study From Best-Diab 2 (Borneo Wetland Study on Diabetes 2).

Subjects of this study were chosen with non-randomized purposive sampling. Eligible subjects were men and women ≥18 years old, consented to participate in the study, that has been diagnosed

with diabetes mellitus. Informed consent about patient's health data was obtained from all the study subjects.

Data were acquired from patients who frequently visited metabolic endocrine polyclinic diabetes mellitus in Ulin Hospital Banjarmasin. Interview was conducted on the patients to gain information of their lifestyle, socioeconomic status, and history of disease. Demographic data and medical history were obtained by a personal interview and by review of the patient's medical records. Included examinations were microvascular complication such as retinopathy diabetic, neuropathy diabetic, nephropathy diabetic, erectile dysfunction and also macrovascular complication such as Coronary Artey Disease (CAD), stroke, Diabetic Foot Ulcer (DFU), and hypertension.

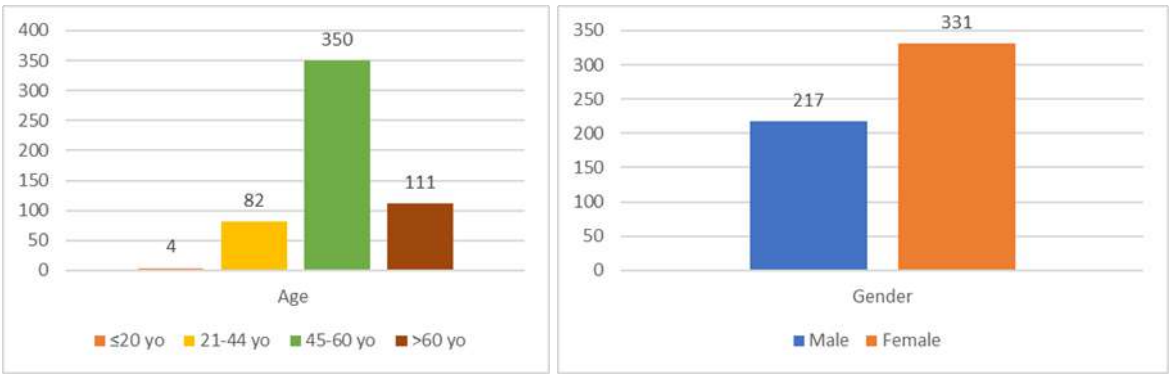
## RESULTS

### Subjects Characteristics

A total of 545 data were collected from endocrine and metabolic polyclinic in Ulin Hospital Banjarmasin visit during the period of 2019- 2022. Demographic data and medical history were obtained by a personal interview and by review of the patient's medical records. Age, gender, duration of DM, and HbA1c level were tabulated. The sample also categorized into groups of microvascular complications (retinopathy, neuropathy, nephropathy, erectile dysfunction) and macrovascular (stroke, coronary heart disease, PAD/Peripheral Artery Disease).

Table 1. Basic Characteristics of Research Subjects

| Characteristic | Amount | Percentage |
|---|---|---|
| Age | | |
| ≤20 y.o | 4 | 0,74% |
| 21-44 y.o | 82 | 14,99% |
| 45-60 y.o | 350 | 63,98% |
| >60 y.o | 111 | 20,29% |
| Gender | | |
| Male | 217 | 39,5% |
| Female | 331 | 60,5% |
| Duration of DM | | |
| < 5 years | 235 | 43,1% |
| 5-10 years | 127 | 23,3% |
| >10 years | 183 | 33,6% |
| HbA1c level | | |
| <7% | 57 | 10,9% |
| 7-9% | 201 | 41,6% |
| >9% | 225 | 47,5% |




(a) (b)

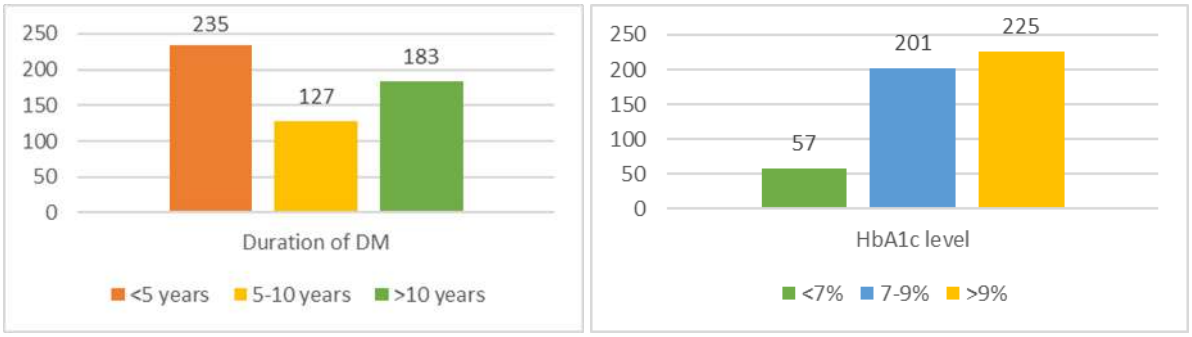
Figure 1. Distribution of Subjects Characteristics (a) by Age and (b) by Gender

Table 1 shows the characteristics of the diabetic population. All cases were considered to have type 2 diabetes The samples were predominantly female (n=331, 60,5%) were diagnosed with diabetes mellitus. The diabetes mellitus group was mostly consisted of individuals aged 45-60 years

(n=350, 63.98%).

Based on the result, it was found that diabetes affected 350 subjects 45-60 years of age (63,98%), mostly in middle adulthood, 82 individuals 21-44 years of age (14,99%) and 111 individuals >60 years of age (20,29%).

The results of this study indicate that the majority of respondents were female suffered from DM (n=331, 60,5%) compared to male (n=217, 39,5%) (Table 1).




(a) (b)

Figure 2. Distribution of Patients (a) by Disease Duration and (b) by HbA1c Level in Diabetes Mellitus Patients

Based on the result, it was found that most patients participating in this study had suffered from DM for less than 5 years (n=235, 43.1%), about 127 patients (23.2%) suffered for 5-10 years, and 183 patients (33,6%) had suffered from DM for more than 10 years.

Based on the result, there are 225 patients (47.5%) had HbA1c levels more than 9%, there are 201 patients (41.6%) who had HbA1c levels between 7-9% and as many as 57 patients (10.9%) have a normal HbA1c level <7% or otherwise controlled.

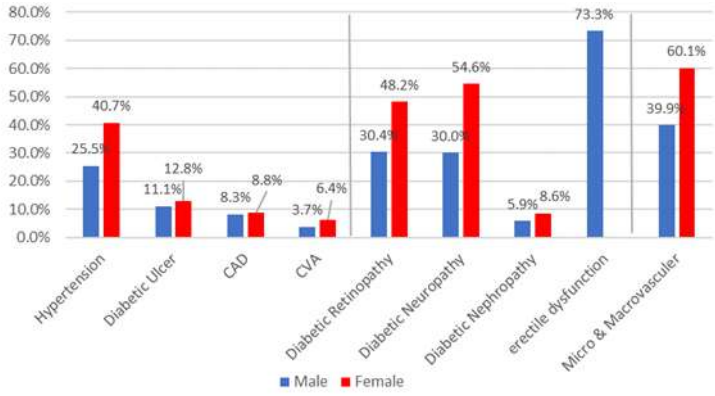



Figure 3. Macrovascular and Microvascular Complication in Diabetes Mellitus Patient

Out of the 545 subjects in this research, there are 421 patients (77.2%) who had a macrovascular complications, there are 479 patients (87%) who had a microvascular complications and there are 381 patients (69.9%) who had both of the complications.

Table 2. Macrovascular and Microvascular Complication

| Characteristic | Amount | Percentage |
|---|---|---|
| **Macrovascular Complication** | | |
| **Hypertension** | | |
| Male | 139 | 25.5% |
| Female | 222 | 40.7% |
| **Total** | 361 | 66.2% |
| **Diabetic Ulcer** | | |
| Male | 61 | 11.1% |
| Female | 70 | 12.8% |
| **Total** | 131 | 23.9 |

| Characteristic | Amount | Percentage |
|---|---|---|
| **Coronary Artery Disease** | | |
| Male | 45 | 8.25% |
| Female | 48 | 8.8% |
| **Total** | 93 | 17.05% |
| **Stroke/Cerebrovascular Accident** | | |
| Male | 20 | 3.66% |
| Female | 25 | 6.42% |
| **Total** | 55 | 10.08% |
| **Microvascular Complication** | | |
| **Diabetic Retinopathy Subjects** | | |
| Male | 166 | 30.4% |
| Female | 263 | 48.2% |
| **Total** | 429 | 78.6% |
| **Diabetic Neuropathy** | | |
| Male | 164 | 30.0% |
| Female | 298 | 54.6% |
| **Total** | 462 | 84.6% |
| **Diabetic Nephropathy** | | |
| Male | 32 | 5.87% |
| Female | 47 | 8.62% |
| **Total** | 79 | 14.49% |
| **Erectile Dysfunction** | | |
| Male | 159 | 73.3% |
| Female | 58 | 26.7% |
| **Total** | 217 | 100% |

**Macrovascular Complications**

There are total of 361 DM patients who also suffer from hypertension, including 139 male patients (25.5%) and 222 patients (40.7%) are female.

Based on the data above, it shows that there are 131 DM patients (24%) experienced diabetic ulcers, which 61 patients (11.1%) were male and 70 patients (12.8%) were female, while 414 patients (76%) did not experience these complications.

Out of 545 DM patients there are 93 (17.06%) who had coronary heart disease, that consist of 45 male patients (8.25%) and 48 female patients (8.8%). Out of 545 patients, there were 55 (10%) patients who had a stroke that 20 patient (3.66%) are male and 35 patients (6.42%) are female.

**Microvascular Complications**

Based on the data above, it shows that there are 429 of DM patients had complications of diabetic retinopathy which consisted of 166 male patients (30.4%) and 263 women patients (48.2%), while 118 patients (21.6%) did not experience these complications.

it was found that neuropathy diabetics patients was higher for amount of 462 patients that consist of 164 men patients (30%) and 298 woman patients (54.6%), while those 55 patients (25,4%) were not found any of diabetic neuropathy.

Based on the result, it was found that 79 patients (14.5%) had nephropathy diabetic consisting of 32 men (5.87%) and 47 woman (8.62%), while those who did not have diabetic nephropathy was found in 466 patients (85.5%).

Based on the result, it was found that among of 217 male patients, there were 159 patients (73.3%) that had erectile dysfunction (ED).

**DISCUSSIONS**

In this study, the most common age group was 45-60 years. Previous study conducted by Sudoyo et al supports this finding by stating that the age group of more than or equal to 40 years was the common stage where people mostly suffer from diabetes. As age increases, the prevalence of impaired glucose tolerance is also increased. Older ages could be at risk because physiological

performance at the ages will decrease and cannot control the body's function optimally, thereby decreasing insulin resistance that leads to high blood glucose levels. The aging process that takes place after the age of 30 causes anatomical, physiological and biochemical changes in the body. The change starts at the cellular level, continues at the tissue level and finally at the level of organs that can affect homeostatic function this include pancreatic beta cells that produce the hormone insulin, cells target tissues that produce glucose, the nervous system, and other hormones that affect glucose levels[2.3].

Women were found more than men in this study. Some research finds that women were 3-7 times more likely to suffer from DM compared to men. Differences in body fat composition and sex hormone levels may be the reasons on why women have more potential to suffer from DM than men. A greater percentage of body fat in women compared to men which is one of the factors that can reduce sensitivity to the workings of insulin in the muscles and liver. Furthermore, women are more sensitive to social contexts such as education, income, and employment as an increased risk of diabetes[4].

The duration of diabetes mellitus < 5 years is the highest compared to the others. Duration of diabetes is one of the most determinants factors of complication risk. Furthermore, some study mentions that sufferers had a high risk of complications due to prolonged diabetes duration. Functional capacity, psychological, level of health, and level of welfare of patients can be affected by diabetes duration. Microvascular and macrovascular complications will be experienced by patients for a long time and then will cause physiological changes when blood glucose levels are high.

Patients with HbA1c more than 9% were the most frequently found in this study (41.6%). The concentration of HbA1c in the blood depends on both the lifespan of red blood cells and the blood glucose concentration. HbA1c level measurement can provide an overview of the average level of glucose in the blood for about 2-3 months. Measuring the HbA1c value is commonly used in DM patients as a marker of glycemic control and as a marker for changing the treatment when needed. Chronic DM complications have been investigated both in general and in relation to HbA1c value, several studies show that lowering HbA1c levels will be associated with a decrease in the incidence of complications in DM patients[2.4].

Diabetes mellitus (DM) is associated with a few vascular and non-vascular complications. Generally, the injurious vascular effects of hyperglycemia are separated into microvascular complications (diabetic nephropathy, neuropathy, and retinopathy), and macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke)[5]. According to Dorsey et al, some factor that can cause patients to experience complications including increased of age, duration of diabetes mellitus, hypertension, dyslipidemia, smoking, and high alcohol.

The correlation between hypertension and type 2 DM is very complex. Hypertension and type 2 diabetes are common comorbidities. Hypertension is twice as frequent in patients with diabetes compared with those who do not have diabetes. Moreover, patients with hypertension often exhibit insulin resistance and are at greater risk of diabetes developing than are normotensive individuals.[6] In health, insulin maintains glucose homeostasis by integrated actions on carbohydrate, protein, and lipid metabolism. Loss of sensitivity to aspects of insulin action (insulin resistance) principally affects the liver, muscle, and adipose tissues and is selective for glucose and lipid metabolism, eg, sparing insulin's action to retain sodium in the distal tubule leads to compensatory hypersecretion of insulin to maintain homeostasis.

The major cause of morbidity and mortality in diabetes is cardiovascular disease, which is exacerbated by hypertension. Accordingly, diabetes and hypertension are closely interlinked because of similar risk factors, such as endothelial dysfunction, vascular inflammation, arterial remodeling, and atherosclerosis. There is also substantial overlap in the cardiovascular complications of diabetes and hypertension related primarily to microvascular and macrovascular disease[3.4].

Diabetic foot ulcers represent a very complex and difficult to treat wound. More than half of diabetic ulcers become infected, and about 20% lead to some level of amputation which has a large long-term impact on morbidity, mortality, and quality of life of people with diabetes mellitus. The previous study by Purwanti (2013) discussed risk factors for developing foot ulcers occur in patients with Diabetes Mellitus at the Surakarta Hospital, it is known that DM patients who experience diabetic ulcers are influenced by poor of foot care, motor neuropathy, Peripheral Artery Disease, lacked blood sugar control and visual disturbances[6].

Although the precise mechanisms through which diabetes increases the likelihood of atherosclerotic plaque formation are not completely defined, the association between the two is profound. The mechanism involves the activation of NFB which leads on the expression of several inflammatory genes, including adhesion molecules that facilitate monocyte adhesion to arterial endothelial cells. The presence of atherosclerotic plaque will blockage the blood flow and can't supply organs properly and produce damage to some of the involved organs. If plaque is released, then it will flow to smaller blood vessels and form a thrombus. When it hits the heart, it will cause coronary artery disease which leads to heart failure[7].

Cerebrovascular complications make diabetic patients more susceptible to a stroke event. Diabetes can cause pathologic changes in blood vessels at various locations and can lead to stroke if cerebral vessels are directly affected. Uncontrolled Hyperglycemia is a significant predictor of fatal and nonfatal stroke[5.7].

Previous study of Putri et al. shows that patients with a duration of more than 5 years have more diabetic retinopathy experienced. Research conducted by Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) showed that the prevalence of patients suffering from diabetic retinopathy increased by 8% after 3 years of DM, then increased up to 25% after 5 years, 60% after 10 years, and 80% after 15 years. The most significant factor in the development and progression of DR in people with diabetes appears to be poor glycemic (blood sugar) control. Under hyperglycemic conditions, which are frequently seen in people with diabetes, impairment of retinal blood flow, increased inflammatory cell adhesion to retinal blood vessels, and capillary blockage can result in hypoxia and damage to the retina. Prolonged hyperglycemic conditions also trigger the formation of many free radicals such as advanced glycation end (AGE) product, sorbitol and induced reactive oxygen species by excess blood glucose in the body of diabetics. These free radicals will make circulatory disturbances, hypoxia and retinal inflammation[8.9].

Approximately one half of people with diabetes have some form of peripheral neuropathy (PN), either polydiabetic or monodiabetic neuropathy. Previous study conducted by Mildawati et al supports this finding by stating that most of diabetic patients (n=44, 53%) have diabetic neuropathy. Diabetic neuropathy is a most common and serious complication in type 2 diabetes mellitus. the mechanisms of hyperglycemia-induced polyol pathway, injury from AGEs, and enhanced oxidative stress have been implicated in its pathogenesis. The damage to peripheral nerves may be mediated by effects on nerve tissue or by endothelial injury or vascular dysfunction. Complications of neuropathy can be experienced by diabetics of all ages. Research by Mildawati et al. showed that in 21 people aged >65 years, there were 19 people (90.5%) who had diabetic neuropathy. While a young adults group (18-44 years) are more likely to have no diabetic neuropathy (n=19, 79.2%)[10].

According to research that carried out at Dr. M. Djamil Hospital Padang, all of patients with nephropathy (n=26, 70.1%) had poor blood glucose levels (> 200 ng/dL). Diabetic nephropathy (DN) is a serious and progressive complication of both type 1 DM and type 2 DM. In patients with type II diabetes, the incidence of diabetic nephropathy ranges from 12 to 16% of patients that diagnosed at age >40 years. As many as 7% of patients with type 2 diabetes may already have microalbuminuria at the time they are diagnosed with diabetes, and the incidence of proteinuria also increased from those who had been diagnosed for 20-25 years. And for about 5-10% of Type II DM patients with diabetic nephropathy will develop kidney failure.11 According to research at Nagaswidak Health Center Indonesia, they found that about 43.3% elderly suffer from DM experience erectile dysfunction, this is associated with the increasedo of fasting plasma insulin, as well as free testosterone levels and lower dihydrotestosterone[12].

Erectile dysfunction or the inability to get or maintain an erection firm enough for sex is common in men who have diabetes, especially those with type 2 diabetes. It can stem from damage to nerves and blood vessels caused by poor long-term blood sugar control. In a normal conditions, endothel produce nitric oxide (NO) which is useful in dilating blood vessels, including in the penis. Hyperglycemia will trigger excessive secretion of arginase II enzyme in the corpus cavernosum which causes inhibition of NO activity which is required in vascular smooth muscle contractility. As a result, penile blood vessels are difficult to dilate and blood flow to the erectile organs decreases so that it can trigger occurrence of Erectile Dysfunction[13].

## CONCLUSION

The most common macrovascular complication is hypertension and the majority of patients are women. Meanwhile, the most common microvascular complications were diabetic neuropathy in the majority of women, and erectile dysfunction in all male patients.

However, these results still require further research to confirm our results. The addition of other factors that can affect the risk of microvascular and macrovascular complications. The prospective study design appears to be more accurate for assessing causation.

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## REFERENCES

1. Setiati S, Alwi I, Sudoyo AW, Stiyohadi B, Syam AF. Buku Ajar Ilmu Penyakit Dalam Jilid I. VI. Jakarta: Interna Publishing; 2014:1132-53.
2. Komariah, Rahayu S. Hubungan Usia, Jenis Kelamin dan Indeks Massa Tubuh Dengan Kadar Glukosa Darah Puasa pada Pasien Diabetes Mellitus Tipe 2 di Klinik Pratama Rawat Jalan Depok. Jurnal Kesehatan Kusuma Husana. 2020.
3. Saputri RD. Komplikasi Sistemik pada Pasien Diabetes Mellitus Tipe 2. JIKSH. 2020;11(1).
4. Jelantik GI, Haryati E. Hubungan Faktor Risiko Umur, Jenis Kelamin, Obesitas, dan Hipertensi Dengan Kejadian Diabetes Mellitus Tipe II di Wilayah Kerja Mataram. Media Bina Ilmiah. 2013.
5. Yuhelma, Hasneli Y, Nauli FA. Identifikasi dan Analisis Komplikasi Makrovaskuler dan Mikrovaskuler pada Pasien Diabetes Mellitus. 2015;2(1).
6. Oktorina O, Aria Wahyuni, Ervina Yanti Harahap. Faktor yang Berhubungan dengan Perilaku Pencegahan Ulkus Diabetikum pada Penderita Diabetes Mellitus. *REAL in Nursing Journal* (RNJ). 2019;2(3).
7. Suryanegara NM, Acang N, Suryani YD. Kajian Mengenai Komplikasi Makrovaskular pada Pasien Diabetes Mellitus Tipe 2. *Prosiding Kedokteran*. 2021;7(1).
8. Dewi PN, Fadrian, Havriza V. Profil Tingkat Keparahan Retinopati Diabetik Dengan Atau Tanpa Hipertensi di Rsup Dr. M. Jamil Padang. *Jurnal Kesehatan Andalas*. 2019; 8(2).
9. Sitompul R. Retinopati Diabetik. *J Indon Med Assoc*. 2011;61(3): 37-41.
10. Putri RN, Waluyo A. Faktor Resiko Neuropati Perifer Diabetik pada Pasien Diabetes Mellitus Tipe 2 : Tinjauan Literature. *Jurnal Keperawatan Abdurrab*. 2020;3(2).
11. Harie SE, Decroli E, Afriwardi. Faktor Risiko Pasien Nefropati Diabetik yang Dirawat di Bagian Penyakit Dalam Rsup Dr. M. Jamil Padang. *Jurnal Kesehatan Andalas*. 2018;7(2).
12. Wowor JA, Tendean LE, Rumbajan JM. Pengaruh Diabetes Terhadap Kejadian Disfungsi Ereksi. *eBiomedik*. 2021; 9(2): 222-28.
13. Derosa G, Tinelli C, D'Angelo A, Ferrara G, Bonaventura A, Bianchi L, et al. Glyco-Metabolic Profile Among Type 2 Diabetic Patients With Erectile Dysfunction. *Endocr J*. 2012;59(7): 611–9.